Novel Reactions of Carbon Suboxide. VI. Synthesis of 2-Oxo-1-benzopyran- and 2-Oxoquinoline-3-carboxylic Acid Hydrazides [1]

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A simple, one step synthesis of 2-oxo-1-benzopyran- and 2-oxoquinoline-3-carboxylic acid hydrazides from carbon suboxide and hydrazones is described.

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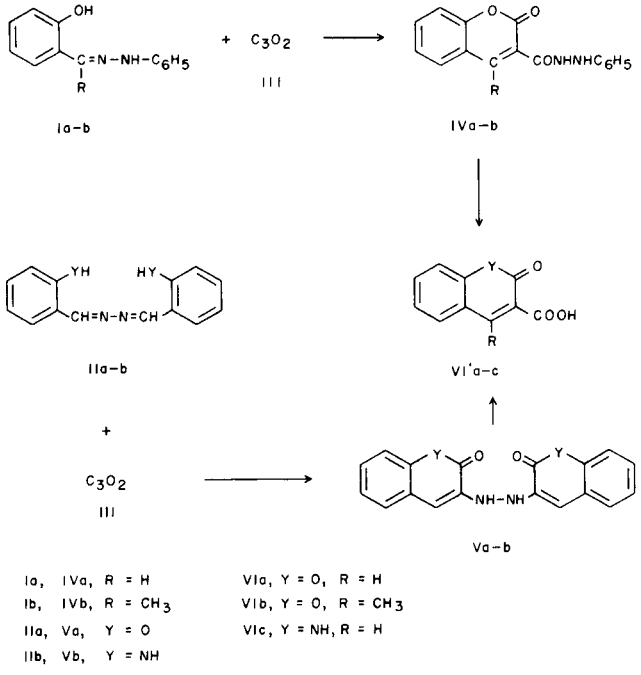
In recent reports on the synthesis of heterocyclic compounds starting from carbon suboxide and azomethynes or 2-hydroxyaryloximes, we described the preparation of some 2-oxo-2*H*-1-benzopyran [2] and 2-oxo-1,2-dihydroquinoline derivatives [3].

Our interest in developing convenient syntheses of benzocondensed heterocyclic compounds with oxygen or nitrogen atoms from readily available starting materials has continued, primarily because of their potential biological activity.

In this communication we describe a convenient single step synthesis of 2-oxo-1-benzopyran-IVa-b and 2-oxoquinoline-3-carboxylic acid hydrazides Va-b, which consists of the condensation of hydrazones Ia-b, IIa-b with carbon suboxide (III) (Scheme 1). The yields of the products were reasonably good. The structures assigned to all compounds synthesized were based on their ir, nmr, mass spectral data and elemental analysis. In fact, the mass spectra of IVa, IVb, Va, Vb show molecular ion at m/e 280, 294, 376, 374, respectively, and abundant ions characteristic of M^+ -NHNHR and M^+ -CONHNHR. The nmr spectra show for all compounds both aromatic signals at δ 6.6-7.65 ppm, and NH amidic signals between δ 6.9 and 10.3 ppm; moreover, IVa, Va, Vb show a signal between δ 8.1 and 8.8 ppm attributable to proton 4; IVa, IVb exhibit also NH-Ar signal and IVb shows a signal attributable to methylic protons. Finally, the ir spectra show a characteristic NH amidic band between 3450 and 3360 cm^{-1} and C=O bands between 1760 and 1680 cm^{-1}.

All the compounds were further characterized by hydrolysis to the corresponding carboxylic acids Va-c.



EXPERIMENTAL

Literature procedures were followed in the preparation of carbon suboxide (III) [4] and hydrazones Ia-b, IIa-b [5-8].

Mass spectra were measured with an Hitachi Perkin-Elmer RMU-6D spectrometer at 70 eV. The ^1H nmr spectra were recorded on a Varian FT 80A spectrometer and the chemical shifts were determined using tetramethylsilane as the interanal standard. The ir spectra were obtained on a Perkin-Elmer model 157G spectrophotometer, using nujol mulls. Melting points were determined by the capillary method on an electrically heated melting point apparatus (Electrothermal) and are uncorrected. Elemental analyses for C,H,N were carried out on a Carlo Erba model 1106 Elemental Analyzer.

2-Oxo-2*H*-1-benzopyran-3-carboxylic Acid 2-Phenylhydrazide (IVa).

To a stirred solution of Ia (16 mmoles) in dry ether (300 ml), III (16 mmoles) was added during one hour at −70°. When the addition was complete, the mixture was stirred at 0° for 8 hours and at room temperature for 3 days. The solvent was evaporated *in vacuo* and the residue was purified by chromatography on a silica gel column using petroleum ether (40-70° pb)-ether (5:1) as the eluent giving pale brown crystals (67%), mp 175-176°; ir: 3420 (NH), 1740, 1700, 1680 cm^{-1} (C=O); nmr (deuteriochloroform): δ 10.21 (d, 1H, N*H*-CO, deuterium oxide exchanged), 8.01 (s, 1H, H-4), 7.05 (m, 9H, Ar-*H*), 4.43 (d, 1H, N*H*-Ar, deuterium oxide exchanged); ms: m/e 280 (M^+), 173 (M^+ -107), 145 (M^+ -135).

Anal. Calcd. for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 10.00. Found: C, 68.46; H, 4.25; N, 10.26.

This compound, after hydrolysis with 20% aqueous sodium hydroxide, furnished the acid VIa.

4-Methyl-2-oxo-2*H*-1-benzopyran-3-carboxylic Acid 2-Phenylhydrazide (IVb).

A solution of Ib (16 mmoles) in dry ether (300 ml) was treated at −70° with III (16 mmoles) and worked up in the same manner described above. The product afforded pale brown crystals (54%), mp 177-178°; ir: 3360 (NH), 1760, 1700, 1690 cm^{-1} (C=O); nmr (deuteriochloroform): δ 7.03 (m, 9H, Ar-*H*), 6.87 (d, 2H, N*H*-N*H*, deuterium oxide exchanged), 2.18 (s, 3H, CH_3); ms: m/e 294 (M^+), 187 (M^+ -107), 159 (M^+ -135).

Anal. Calcd. for $C_{17}H_{14}N_2O_3$: C, 69.37; H, 4.79; N, 9.52. Found: C, 69.61; H, 5.01; N, 9.38.

This compound, after hydrolysis with 20% aqueous sodium hydroxide, furnished the acid VIb.

2-Oxo-2*H*-1-benzopyran-3-carboxylic Acid 2-(2-Oxo-2*H*-1-benzopyran-3-carbonyl)hydrazide (Va).

To a stirred solution of IIa (16 mmoles) in dry benzene-toluene (5:1) (400 ml) III (32 mmoles) was added during one hour at −70°. When the addition was complete, the mixture was stirred at 0° for 4 hours and then kept with stirring at room temperature for 36 hours. The reaction solution was evaporated *in vacuo* and the residue purified by column chromatography, using silica gel, eluent petroleum ether (40-70° bp)-ether (5;1), to give yellow crystal (65%), mp 178-179°; ir: 3400 (NH), 1730, 1700, 1685 cm^{-1} (C=O); nmr (DMSO-d_6): δ 8.64 (s, 2H, H-4), 7.15 (d, 2H, N*H*-N*H*, deuterium oxide exchanged), 7.07 (m, 8H, Ar-*H*); ms: m/e 376 (M^+), 173 [(M^+ -30)/2], 145 [(M^+ -86)/2].

Anal. Calcd. for $C_{20}H_{12}N_2O_6$: C, 63.83; H, 3.21; N, 7.44. Found: C, 64.00; H, 3.50; N, 7.24.

This compound, after hydrolysis with 20% aqueous sodium hydroxide, furnished the acid VIa.

2-Oxo-1,2-dihydroquinoline-3-carboxylic Acid 2-(2-Oxo-1,2-dihydroquinoline-3-carbonyl)hydrazide (Vb).

A stirred solution of IIb (16 mmoles) in dry benzene-toluene (5:1) was treated at −70° with III (32 mmoles) and worked up in the same manner described for Va. The product afforded yellow crystals (77%), mp 244-245°; ir: 3450 (NH), 1740, 1700, 1685 cm^{-1} (C=O); nmr (DMSO-d_6): δ 11.2 (s, 2H, H-1, deuterium oxide exchanged), 8.79 (s, 2H, H-4), 8.12 (d, 2H, N*H*-N*H*, dueterium oxide exchanged), 7.23 (m, 8H, Ar-*H*); ms: m/e 374 (M^+), 172 [(M^+ -30)/2], 144 [(M^+ -86)/2].

Anal. Calcd. for $C_{20}H_{14}N_4O_4$: C, 64.16; H, 3.77; N, 14.97. Found: C, 63.95; H, 3.65; N, 14.81.

This compound, after hydrolysis with 20% aqueous sodium hydroxide furnished the acid VIc.

REFERENCES AND NOTES

[1] This work was supported in part by the National Research Council (CNR), Rome, Italy.

[2] L. Bonsignore, S. Cabiddu, G. Loy and M. Secci, *Tetrahedron Letters*, **24**, 5013 (1983).

[3] L. Bonsignore, S. Cabiddu, G. Loy and M. Secci, *Synthesis*, 266 (1984).

[4] L. Crombie, P. A. Gilbert and R. P. Houghton, *J. Chem. Soc. (C)*, 130 (1968).

[5] E. Fischer, *Chem. Ber.*, **17**, 572 (1884).

[6] Y. Tahara, *Chem. Ber.*, **25**, 1306 (1892).

[7] H. Cajar, *Chem. Ber.*, **31**, 2803 (1898).

[8] K. Miyatake, *J. Pharm. Soc. Japan*, **72**, 1162 (1952).